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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,518	08/24/2001	Mark J. Jaroszeski	93004	2429

7590 05/09/2002

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	6

DATE MAILED: 05/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,518	JAROSZESKI ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-20 are pending in the application.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 11-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding the instant claims which are drawn to a "system" for facilitating a delivery of a desired molecule into a target tissue comprising a "means for introducing" the molecule and a "means for applying a substantially continuous low-level electric field" and further comprising a means for constructing a plasmid; It is noted that 35 U.S.C. 112 sixth paragraph states,

> "An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof."

The only structure or material of the system described in the specification as a means for delivering the molecule of interest is found on page 7, lines 12-17, which discloses that the means for delivering may include syringe injection, jet injection, oral dosing, or other means known in the art (emphasis added). Therefore, the "system" claims encompass any known mechanism of delivery. However, the fact that claim encompasses any known means also renders the claim (and the depending claims) indefinite because the metes and bounds of claim cannot be determined. Also, there is no description in the specification of the structures or

materials of every known means of delivery, further rendering the instant claims indefinite. For examination purposes, the claims are interpreted to encompass any means of delivery.

Furthermore, there is no specific disclosure in the specification regarding the structure or material of the system comprising a means for applying a substantially continuous low-level electric field. There is only a general description of the electric fields that are applied (see page 6, middle paragraph; and Examples 1-3, pages 8-11). Therefore, the instant claims are indefinite because there is no specific description of the structure or material of the system comprising a means of applying an electric field, as required (see 35 U.S.C. 112, sixth paragraph) rendering the claims vague and indefinite. For examination purposes, the claims are interpreted to encompass any means of applying the low-level electric field described in the specification.

Finally, claim 19 encompasses a system comprising a "means for constructing a plasmid". The specification does not disclose any steps, methods or materials required to construct the plasmid. Therefore it is unclear what is meant by a system comprising a means for constructing a plasmid. For instance, a Biotechnology company (such as Promega) is capable of manufacturing plasmids; a tube comprising nucleic acids and appropriate enzymes could be a means for constructing a plasmid; and a molecular biology lab comprising lab technicians and the appropriate reagents is also a means for constructing a plasmid. Therefore it is unclear what a system comprising a means for constructing a plasmid encompasses. For examination purposes, the claims are interpreted to encompass any means for constructing a plasmid.

1. Claims 9 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite the phrase, "a plasmid comprising a DNA and cDNA that codes for a desired molecule." This phrase renders the claims indefinite because it is unclear how the DNA/cDNA "codes for" a desired molecule. An amendment to the claims, such as replacing "codes for" with "encoding", is required.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 4-11 and 14-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Lucas et al. (DNA and Cell Biol. Vol. 20(3):183-8; March 2001).

Lucas teaches a method and for facilitating a delivery of a desired molecule, here a plasmid encoding Luciferase (see p. 184, second column), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see Fig. 2 and Table 2);

Wherein the low-level electric field has a field strength comprising 200V/cm or less (see Fig 2 and Table 2);

Wherein the electric field comprises a square pulse waveform and a waveform having a nongeometrically characterizable shape, here described as an exponentially enhanced pulse (EEP)(see Fig 1 and Table 2);

Wherein the introducing step comprises syringe injection (see p. 184, second column);

Wherein the target tissue is skin or muscle (see Fig 2 and Fig. 4).

Lucas also teaches a system comprising a means for facilitating a delivery of a desired molecule, here a plasmid encoding Luciferase (see p. 184, second column), into a target tissue comprising a cell; and further comprising a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see Fig. 2 and Table 2);

Wherein the low-level electric field has a field strength comprising 200V/cm or less and is applied in series of electric pulses (see Fig 2 and Table 2);

Wherein the electric field comprises a square pulse waveform and a waveform having a nongeometrically characterizable shape, here described as an exponentially enhanced pulse (EEP)(see Fig 1 and Table 2);

Wherein the means of introducing the molecule comprises syringe injection (see p. 184, second column);

Wherein the target tissue is skin or muscle (see Fig 2 and Fig. 4).

3. Claims 1, 4-5 and 14, 15 and 16-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Heller et al. (DNA and Cell Biol. Vol. 20(1):21-6; January 2001).

Heller teaches a method for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase and IL-12 (see p. 22, second column), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see p. 22, second column; and Fig. 1);

Wherein the low-level electric field has a field strength comprising 200V/cm or less and is applied in series of electric pulses (see Fig 1);

Wherein the introducing step comprises injection (see p. 23, first column);

Wherein the target tissue is skin (see Fig 1 and Fig 2).

Heller also teaches a system comprising a means for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase and IL-12 (see p. 22, second column), into a target tissue comprising a cell; and further comprising a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see p. 22, second column; and Fig. 1);

Wherein the low-level electric field has a field strength comprising 200V/cm or less and is applied in series of electric pulses (see Fig 1);

Wherein the means of introducing the molecule comprises injection (see p. 23, first column);

Wherein the target tissue is skin (see Fig 1 and Fig 2).

4. Claims 1, 4-5 and 14, 15 and 16-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Bettan et al. (Bioelectrochemistry Vol. 52:83-90; September 2000).

Bettan teaches a method for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase and β-galactosidase (see p. 84, under Plasmids; Fig. 1; and Fig. 6), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see abstract, p. 84, first column; and p. 89, first column);

Wherein the low-level electric field has a field strength comprising 200V/cm or less and is applied in series of electric pulses (see Fig 1);

Wherein the introducing step comprises syringe injection (see p.84, last paragraph);

Wherein the target tissue is tumor tissue (see Fig 1).

Bettan also teaches a system comprising a means for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase and β-galactosidase (see p. 84, under Plasmids; Fig. 1; and Fig. 6), into a target tissue comprising a cell; and further comprising a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry

of a desired molecule into an interior of a cell (for example, see abstract, p. 84, first column; and p. 89, first column);

Wherein the low-level electric field has a field strength comprising 200V/cm or less and is applied in series of electric pulses (see Fig 1);

Wherein the means of introducing the molecule comprises syringe injection (see p.84, last paragraph);

Wherein the target tissue is tumor tissue (see Fig 1).

5. Claims 1, 4-6, 8-11, 14-16 and 18-20 rejected under 35 U.S.C. 102(b) as being anticipated by Mir et al. (PNAS Vol. 96:4262-4267; April 1999).

Mir teaches a method for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase, β-galactosidase and FGF1 (see p. 4263, first paragraph), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, abstract; and Fig 1);

Wherein the low-level electric field has a field strength comprising 200V/cm or less(see Fig 1);

Wherein the electric field comprises a square pulse waveform (see p. 4263, first column and Fig 1);

Wherein the introducing step comprises syringe injection (see p. 4263, first column);

Wherein the target tissue is muscle (see p. 4263, first column and Fig. 2).

Mir also teaches a system comprising a means for facilitating a delivery of a desired molecule, here plasmids encoding Luciferase, β-galactosidase and FGF1 (see p. 4263, first paragraph), into a target tissue comprising a cell; and further comprising a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, abstract; and Fig 1);

Wherein the low-level electric field has a field strength comprising 200V/cm or less(see Fig 1);

Wherein the electric field comprises a square pulse waveform (see p. 4263, first column and Fig 1);

Wherein the method of introducing the molecule comprises syringe injection (see p. 4263, first column);

Wherein the target tissue is muscle (see p. 4263, first column and Fig. 2).

6. Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hofmann et al. (U.S. Patent 6,055,453, published April 25, 2000).

Hofmann teaches a method for facilitating a delivery of a desired molecule, here nucleic acids, antisense nucleic acids, Ribozymes, polypeptides, and polynucleotides (such as expression vectors) encoding metabolic enzymes and proteins(see col. 12, lines 14 and 34; col. 13, lines 13, 24 and 31-31), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the

cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example see col. 1, lines 6-13; col. 10, lines 3-56; and col. 11, lines 63-65);

Wherein the low-level electric field has a field strength comprising 10V/cm-20kV/cm and for a duration of 10μs-100ms (see col. 10, lines 3-41);

Wherein the electric field comprises multiple square pulse waveforms (see col.10, line 55-56);

Wherein the introducing step comprises needle injection (i.e. syringe) (see col. 13, lines 31-45 and);

Wherein the target tissue is skin, tumor, muscle, ovary, prostate, lung, heart, kindney, colon, testis, melanoma, etc. (see col. 14, lines 10-30).

And wherein the method further comprises a means for constructing a plasmid comprising a DNA and cDNA encoding a molecule of interest (see col. 12, line 61-col. 13, line 11).

Hofmann also teaches a system comprising a means for facilitating the delivery of a desired molecule, here nucleic acids, antisense nucleic acids, Ribozymes, polypeptides, and polynucleotides (such as expression vectors) encoding metabolic enzymes and proteins(see col. 12, lines 14 and 34; col. 13, lines 13, 24 and 31-31), into a target tissue comprising a cell; and a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example see col. 1, lines 6-13; col. 10, lines 3-56; and col. 11, lines 63-65);

Wherein the low-level electric field has a field strength comprising 10V/cm-20kV/cm and for a duration of 10μs-100ms (see col. 10, lines 3-41);

Wherein the electric field comprises multiple square pulse waveforms (see col.10, line 55-56);

Wherein the means for introducing the molecule comprises needle injection (i.e. syringe) (see col. 13, lines 31-45 and);

Wherein the target tissue is skin, tumor, muscle, ovary, prostate, lung, heart, kidney, colon, testis, melanoma, etc. (see col. 14, lines 10-30);

And wherein the system comprises a means for constructing a plasmid comprising a DNA and cDNA encoding a molecule of interest (see col. 12, line 61-col. 13, line 11).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell, Ph.D.
May 1, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER